

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-6, 12, 45, 46, 48-57, 59-64, and 67-77 are pending in the application, with claims 1-4, 45, 54, 64 and 74 being the independent claims. Claims 45, 54, 55, 61, 64, and 70-73 are sought to be amended by the present amendment. Claims 7-11, 13-44, 47, 58, and 65-66 were previously cancelled without prejudice to or disclaimer of the subject matter therein. Claims 1-6, 12, and 74-77 are withdrawn from consideration.

Claims 45, 54, 55, 61, 64, and 70-73 are sought to be amended. Specifically, claims 45, 54, and 64 have been amended to recite a specific function. For example, Applicants have amended claim 45 to recite that the CYK-4 protein, fragment, or variant stimulates GTP hydrolysis by the Rho family GTPase in the absence of the compound. Applicants have also amended claim 54 to recite that the CYK-4 protein, fragment, or variant binds the MKLP1 protein subfamily member in the absence of the compound, and claim 64 to recite that the first CYK-4 protein, fragment, or variant binds to the second CYK-4 protein, fragment, or variant in the absence of the compound. Support for the amendment to claim 45 can be found in the specification, for example, at page 28, lines 7-10. Support for the amendment to claim 54 can be found in the specification at page 31, line 13, to page 32, line 6, and in Example 8, at pages 67-69, while support for the amendment to claim 64 can be found in the specification at page 33, lines 18-25, and in Example 11, at pages 75-77.

Claims 45, 54, and 64 have also been amended to recite the phrase "wherein the stringent conditions comprise (i) overnight incubation at 42 °C in a solution comprising

50% formamide, 5x SSC, wherein 1 x SSC comprises 150 mM NaCl and 15 mM trisodium citrate, 50 mM sodium phosphate, pH 7.6, 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA, followed by (ii) washing in 0.1x SSC at about 65 °C." Support for this amendment can be found in Applicants' specification at page 21, lines 14-21. Claims 45, 54 and 64 have also been amended to correct punctuation by replacing with a comma the semicolon following each CYK-4 protein member in the Markush group in each claim.

Lastly, claims 45, 54, 55, 61, and 64 have been amended to strictly conform to proper U.S. claim format by replacing the phrase "fragment of the CYK-4 protein" with the phrase "a fragment of the CYK-4 protein" or the phrase "the fragment of the CYK-4 protein," by inserting either "a" or "the" immediately prior to "fragment of the CYK-4 protein." In addition, Applicants have amended claims 64 and 70-73 to replace "fragment of the first CYK-4 protein" with "a fragment of the first CYK-4 protein" or "the fragment of the first CYK-4 protein," and/or to replace "fragment of the second CYK-4 protein" with "a fragment of the second CYK-4 protein" or "the fragment of the second CYK-4 protein," in a similar manner. Applicants have also amended claim 61 to replace "fragment of the MKLP1 protein" with "the fragment of the MKLP1 protein," again, by inserting "the" immediately prior to "fragment of the MKLP1 protein."

These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***I. Rejection under 35 U.S.C. § 112, First Paragraph, Scope of Enablement***

The Examiner rejects claims 45, 46, 48-57, 59-64, and 67-73 under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a method for identifying a compound having the potential to inhibit cytokinesis employing a CYK-4 protein set forth in SEQ ID NOs 2, 4, or 6, allegedly does not reasonably provide enablement for a method for identifying a compound having the potential to inhibit cytokinesis employing any other CYK-4 proteins. According to the Examiner, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. (Office Action, at page 2, line 14, to page 3, line 6.) Applicants respectfully traverse the rejection.

Specifically, the Examiner states that:

Claims 45, 54, and 64 recite variants of human CYK-4 (SEQ ID NO:2) and murine CYK-4 (SEQ ID NO:4) that are encoded by nucleic acids hybridizing under stringent conditions to a polynucleotide having a nucleotide sequence set forth in SEQ ID NO:1 or SEQ ID NO:3. Claims 48, 59, and 67 recite variants of human CYK-4 (SEQ ID NO:2). The specification only provides a single species of CYK-4 for human CYK-4 of SEQ ID NO:2 and murine CYK-4 of SEQ ID NO:4. There is no sufficient guidance and/or working examples provided in the specification to make and use variants of the human CYK-4 and murine CYK-4 protein. . . . Moreover, the state of the art is such that determining the specificity of hybridization is empirical by nature and the effect of mismatches is unpredictable . . . . It is well known in the art that hybridisation yields structurally related, but functionally different nucleic acids. In this regard, it is noted that there is no functional limitation for the variant encoded by nucleic acids that are produced by hybridization. Thus, it would take undue experimentation

for one skilled in the art to make and use the claimed methods.

(Office Action, at page 3, line 17, to page 4, line 14.)

In order to satisfy 35 U.S.C. § 112, first paragraph, Applicants must provide sufficient guidance so that one of ordinary skill in the art can make and use the claimed invention. The amount of enabling disclosure must be such that a person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988).

In determining whether a patent application satisfies the enablement requirement under 35 U.S.C. § 112, first paragraph, the Federal Circuit held that "[e]nablement is not precluded by the necessity for some experimentation such as routine screening." *In re Wands*, 858 F.2d 731, 736-737 (Fed. Cir. 1988). However, the experimentation cannot be undue. *Id.* The Federal Circuit also held that "[t]he determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art." *Id.* at 737 (quoting *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (Bd. Pat. App. 1982)). The court states that "[t]he test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Id.*

Applicants assert that they have provided sufficient guidance for one of ordinary skill in the art to make and use the CYK-4 variants recited in the claims at issue without undue experimentation and that the present application enables the full scope of the claims as presently amended.

Hybridization techniques were known to those of skill in the art at the time of filing of the application. See, for example, Sambrook *et al.*, Molecular Cloning, a Laboratory Manual, 2<sup>nd</sup> Ed., Cold Spring Harbor Laboratory Press (1989), at Chapter 11, especially page 11.45. Moreover, the specification defines the term "stringent hybridization conditions" used for producing the CYK-4 variants recited in the claims at issue by listing the specific experimental conditions required for stringent hybridization. See Applicants' specification, at page 21, lines 14-21.

The claims also recite that the CYK-4 variants must contain a specific protein domain relevant to the claimed method. For example, claim 45 recites that the CYK-4 protein, fragment or variant comprises a GTPase activating protein domain; claim 54 recites that the CYK-4 protein, fragment or variant comprises a domain that binds MKLP1 subfamily proteins; and claim 64 recites that the first CYK-4 protein, fragment or variant and the second CYK-4 protein, fragment or variant each comprises a domain that mediates CYK-4 protein self-association. In addition, the specification describes in detail the CYK-4 protein domains recited in the claims at issue. For example, at page 50, lines 1-22, the specification describes the conserved C-terminus GTPase activating protein (GAP) domain, and the amino terminal coiled-coil domain that mediates the interaction of CYK-4 with ZEN-4/MKLP1 and CYK-4 self-association. Fig. 3 D illustrates the correspondence of these conserved domains between the *C. elegans* CYK-4 protein and human CYK-4, indicating which amino acid residues are critical for promoting GTP hydrolysis by a Rho family GTPase and which amino acid residues are critical for promoting the binding of CYK-4 to human CYK-4 and human MKLP1. Thus, Fig. 3D of the specification clearly indicates the amino-terminal CYK-4 protein

domain recited in claims 54 and 64 that is critical for CYK-4/MKLP1 and CYK-4/CYK-4 binding, and the C-terminal GAP domain recited in claim 45 that is critical for GTPase activating activity.

Accordingly, the specification would have provided sufficient guidance to one of skill in the art, at the time of filing the application, for making and using the CYK-4 variants of the claimed methods without undue experimentation.

With respect to the Examiner's statement that there are no "working examples provided in the specification to make and use the variants of the human CYK-4 and murine CYK-4 protein" (Office Action, at page 4, lines 2-4), Applicants note that it is long settled case law that Applicants are not required to provide objective evidence in the form of working examples to enable the claimed invention. In *In re Marzocchi*, 439 F.2d 220, 223 (C.C.P.A. 1971), the court stated that "[t]he first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance."

To expedite prosecution and without acquiescing in the propriety of the rejection, however, Applicants have amended claims 45, 54 and 64 to recite the specific stringent hybridization conditions required for isolating the CYK-4 variants recited in the claims. As claims 46, 48-53, 55-57, 59-63, and 67-73 depend from claim 45, claim 54, or claim 64, these dependent claims also incorporate the stringent hybridization conditions recited in claims 45, 54, and 64. Thus, contrary to the Examiner's statement that "the specificity of hybridization is empirical" (Office Action, at page 4, lines 6-7), the claims at issue, as amended, now specifically recite the hybridization conditions required for producing the claimed variants.

To expedite prosecution and without acquiescing in the propriety of the rejection, Applicants have also amended claims 45, 54 and 64 to recite a specific function that the CYK-4 protein, fragment, or variant used in the each claimed method must exhibit. Specifically, Applicants have amended claim 45 to recite that the CYK-4 protein, fragment, or variant stimulates GTP hydrolysis by the Rho family GTPase in the absence of the compound. Applicants have also amended claim 54 to recite that the CYK-4 protein, fragment, or variant binds the MKLP1 protein subfamily member in the absence of the compound. Lastly, Applicants have also amended claim 64 to recite that the first CYK-4 protein, fragment, or variant binds to the second CYK-4 protein, fragment, or variant in the absence of the compound. Thus, contrary to the Examiner's statement that "there is no functional limitation for the variant encoded by nucleic acids that are produced by hybridization" (Office Action, at page 4, lines 12-13), the claims, as amended, now recite that the CYK-4 protein, fragment or variant must exhibit the specific activity relevant to the claimed method in the absence of the compound being tested.

The Examiner also states that "[t]he amended claims are still broad and encompass a screening method employing any CYK-4 proteins and its fragments" and that "no specific structure of the domain is recited in the claims." (Office Action, at page 3, lines 7-8 and 15-16.)

As discussed above, the claimed methods recite that the CYK-4 protein, fragment or variant contains a specific protein domain relevant to the claimed method (e.g., claim 45 recites that the CYK-4 protein, fragment or variant comprises a GTPase activating protein domain; claim 54 recites that the CYK-4 protein, fragment or variant comprises a

domain that binds MKLP1 subfamily proteins; and claim 64 recites that the first CYK-4 protein, fragment or variant and the second CYK-4 protein, fragment or variant each comprises a domain that mediates CYK-4 protein self-association). In addition, the specification provides ample guidance regarding the amino acids comprising the specific domains recited in the claims at issue. As discussed, for example, at page 50, lines 1-22, and in Fig. 3D, the specification describes the GTPase activating protein (GAP) domain of claim 45, and the amino terminal coiled-coil domain that mediates the interaction of CYK-4 with ZEN-4/MKLP1 and CYK-4 self-association required in the methods of claims 54 and 64, respectively.

Moreover, Applicants note that the GAP domain recited in claim 45 was known to those of skill in the art at the time of filing of the application. See, for example, Van Aelst, L., and D'Souza-Schorey, C., *Genes and Development* 11:2295-2322 (1997), at page 2297, left-hand column, lines 20-22, cited and submitted as Doc. No. AR29 in Applicants' Information Disclosure Statement filed for the captioned application on January 18, 2002.

Applicants believe that they have provided sufficient guidance for one of ordinary skill in the art to make and use the CYK-4 proteins, fragments and variants recited in the claims at issue without undue experimentation and that the present application enables the full scope of the claims as presently amended.

Thus, Applicants believe that the rejection of claims 45, 46, 48-57, 59-64, and 67-73 under 35 U.S.C. § 112, first paragraph (scope of enablement), has been overcome and respectfully request that the Examiner reconsider and withdraw this rejection.



**II. Rejections under 35 U.S.C. § 112, First Paragraph, Written Description**

The Examiner rejects claims 45, 46, 48-57, 59-64, and 67-73 under 35 U.S.C. § 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. (Office Action, at page 4, lines 15-20.) Applicants respectfully traverse this rejection.

Specifically, the Examiner states that the claims "do not require that the fragment of CYK-4 protein or the variants of the CYK-4 protein possess any particular biological activity, nor any particular conserved structure, nor other disclosed distinguishing feature." (Office Action, at page 5, lines 16-18.) The Examiner states further that "[i]n the instant case, only a single species of human CYK-4 protein of SEQ ID NO: 2 and a single species of murine CYK-4 protein of SEQ ID NO: 4 are disclosed" and that "[t]hey are not sufficient to support the genus of variants of human and murine CYK-4 proteins." (Office Action, at page 6, lines 7-10). The Examiner then concludes that "[d]ue to the breadth of the genus of CYK-4 proteins and its fragments and lack of the definitive structural or functional features of the genus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the instantly claimed methods that recite the genus of CYK-4 proteins and its fragments." (Office Action, at page 6, lines 11-15.) However, the Examiner notes in the Office Action at page 6, lines 2-6, citing *Regents of the University of California v. Eli Lilly and Co.* (119 F.3d 1559, 1569 (Fed. Cir. 1997)), that a description of a genus may be achieved several ways, including by the recitation of structural features common to a substantial portion of the genus.

Claims 45, 54, and 64 each recite that the CYK-4 protein, fragment or variant contains a specific protein domain relevant to the method recited in the claim, a common structural feature that each CYK-4 protein, fragment, or variant of the claim possesses. For example, claim 45 recites that the CYK-4 protein, fragment or variant comprises a GTPase activating protein domain; claim 54 recites that the CYK-4 protein, fragment or variant comprises a domain that binds MKLP1 subfamily proteins; and claim 64 recites that the first CYK-4 protein, fragment or variant and the second CYK-4 protein, fragment or variant each comprises a domain that mediates CYK-4 protein self-association.

Moreover, to expedite prosecution and without acquiescing in the propriety of the rejection, Applicants have amended claims 45, 54, and 64 to each recite the specific function exhibited by the CYK-4 protein, fragment, or variant recited in each claim, a common functional feature that each CYK-4 protein, fragment, or variant of the claim possesses. Specifically, Applicants have amended claim 45 to recite that the CYK-4 protein, fragment, or variant stimulates GTP hydrolysis by the Rho family GTPase in the absence of the compound; claim 54 to recite that the CYK-4 protein, fragment, or variant binds the MKLP1 protein subfamily member in the absence of the compound; and claim 64 to recite that the first CYK-4 protein, fragment, or variant binds to the second CYK-4 protein, fragment, or variant in the absence of the compound.

Thus, contrary to the Examiner's assertion that the claims "do not require that the fragment of CYK-4 protein or the variants of the CYK-4 protein possess any particular biological activity, nor any particular conserved structure, nor other disclosed distinguishing feature" (Office Action, at page 5, lines 16-18), the amended claims do, in

fact, recite the each CYK-4 protein, fragment and variant possesses both a structural feature and a functional feature common to the genus of CYK-4 proteins, fragments and variants encompassed by each claim. Accordingly, Applicants believe that one of skill in the relevant art would recognize that the Applicants were in possession of the full scope of the claimed methods.

Applicants believe that the rejection of claims 45, 46, 48-57, 59-64, and 67-73 under 35 U.S.C. § 112, first paragraph (written description), has been overcome and respectfully request that the Examiner reconsider and withdraw this rejection.

### ***III. Rejections under 35 U.S.C. § 112, Second Paragraph***

The Examiner rejects claims 45, 46, 48-57, 59-64, and 67-73 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. (Office Action, at page 6, lines 16-19.)

Specifically, the Examiner states that claims 45, 48, 54, 59, 64 and 67 are indefinite because "they recite ' . . . hybridizes under stringent conditions' without giving the specific conditions for hybridization in the claims. Since neither the art nor the specification provides an unambiguous definition for the term, the claims are indefinite." (Office Action, at page 7, lines 1-4.) The Examiner then indicates that claims 46, 49-53, 55-57, 60-63, and 68-73 are also rejected as depending from the rejected claims. (Office Action, at page 7, lines 4-5.)

Applicants direct the Examiner's attention to page 21, lines 14-21, of the specification, and note that, contrary to the Examiner's assertion, the specification does in

fact provide an unambiguous definition of the phrase "stringent conditions" for hybridization. However, to expedite prosecution and without acquiescing in the propriety of the rejection, Applicants have amended claims 45, 54, and 64 to recite the definition of "stringent hybridization conditions" disclosed in Applicants' specification, at page 21, lines 14-21.

Applicants believe that the rejection of claims 45, 46, 48-57, 59-64, and 67-73 under 35 U.S.C. § 112, second paragraph, has been overcome and respectfully request that the Examiner reconsider and withdraw the rejection.

#### ***IV. Claim Objections - Minor Informalities***

The Examiner objects to claims 45, 54, 61, and 70-73 as containing a typographic error, *i.e.*, containing the phrase "fragment of the CYK-4 protein," which the Examiner indicates should be replaced with the phrase, "a fragment of the CYK-4 protein." (Office Action, at page 7, lines 10-11.)

To expedite prosecution and without acquiescing in the propriety of the rejection, Applicants have amended claims 45, 54, 55, 61, and 64 to replace the phrase "fragment of the CYK-4 protein" with the phrase "a fragment of the CYK-4 protein" or the phrase "the fragment of the CYK-4 protein" by inserting either "a" or "the" immediately prior to "fragment of the CYK-4 protein" in each of these claims. In addition, Applicants have also amended claims 64 and 70-73 to replace "fragment of the first CYK-4 protein" with "a fragment of the first CYK-4 protein" or "the fragment of the first CYK-4 protein," and/or to replace "fragment of the second CYK-4 protein" with "a fragment of the second CYK-4 protein" or "the fragment of the second CYK-4 protein," in a similar

manner. Applicants have also amended claim 61 to replace "fragment of the MKLP1 protein" with "the fragment of the MKLP1 protein" by inserting "the" immediately prior to "fragment of the MKLP1 protein."

Applicants believe that the objection to claims 45, 54, 61, and 70-73 has been overcome and respectfully request that the Examiner reconsider and withdraw the objection.

The Examiner also maintains the previous objection to claims 45, 46, 51-57 60-64, and 67-73 as reciting non-elected subject matter (murine CYK-4, or SEQ ID NO:4). (Office Action, at page 7, lines 7-9.)

Applicants note that in the Office Action dated February 23, 2005, the Examiner agreed to examine all generic linking claims, including the search and examination of claims reciting murine SEQ ID NO:4, if a generic claim is allowed.

***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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